REMARKS

Claims 1-17 and 21-23 were presented for examination and were variously rejected, and the rejection was made final by an Office Action mailed on January 24, 2007. The rejections were traversed in a response electronically filed on March 15, 2007. The obviousness rejection was maintained according to an Advisory Action mailed on April 2, 2007.

The claims were amended in the response filed on March 15, 2007; the Advisory Action indicates that the amendment was entered for purposes of appeal. The present claims correspond to those in the amendment filed on March 15, 2007, and have not been further amended.

Many of the following remarks were presented in a Response to Final Office Action that was electronically filed on March 15, 2007. The Advisory Action mailed on April 2, 2007 indicated that the After Final response had not placed the application in condition for allowance, because the obviousness rejection presented in the Final Office Action had not been overcome. The Advisory Action indicates that a previous rejection under 35 U.S.C. 112 was overcome by the response to the Final Office Action, but indicates that an objection remains outstanding. The following remarks are offered in response to the outstanding grounds for rejection. Reconsideration in view of these remarks is respectfully requested.

Objections to the Claims

The Examiner objected to the claims because they allegedly contain non-elected subject matter. The claims are believed to correspond to the scope of the Group that was elected for examination (Group I, "compounds of formula (I) where no other heterocycle is present"), and this objection is understood to relate to claim scope the Examiner had challenged based on prior art and/or other grounds. The rejection under 35 U.S.C. 112 has been withdrawn. The Applicant understands that the subject matter as claimed, which excludes other heterocycles besides the pyrrolidine ring in formula (I), would be examined if the applicant overcomes the remaining rejection, as provided in 37 C.F.R. § 1.141(a). The applicant respectfully requests withdrawal of the objection in view the following comments.

Rejections based on 35 U.S.C. § 103

Claims 1-17 were rejected as obvious in view of Kuroita, et al., U.S. Patent No. 6,468,998. The applicant pointed out in a previous response that the rejection did not appear to provide proper evidence of a motivation to select the claimed invention under the standards applied in In re Baird. The Examiner alleged that Baird is distinguishable from this case:

> In the instant case, the claimed compounds are *not* more complex that those proposed by Kuroita. One species in particular, corresponds to claimed compounds where n is 0, W is L^2-A^3, L^1 is C(O), X^1 is CR^3, L^2 is CH_2CH_2, A^1, A^2, and A^3 are 4-fluorophenyl, and R^1, R^2 and R^3 are hydrogen. See Example 67, column 30, lines 54-61, and the structure on column 33, lines 1-17. The only difference that is required to meet the scope of claim 1 is for the linking group to be extended or contracted, (L^2 in the instant case and D in Kuroita et al.) to overcome the new proviso… Since Kuroita et al. defines D to be:
>
> > D is optionally substituted linear or branched chain alkylene having 1 to 8 carbon atoms, and when D is branched alkylene, the carbon atoms in the branched chain is optionally bonded further to Ar to form 4- to 8-membered ring, and…
>
> One of skill in the art would take the compound cited above, have motivation to use a different linking group between the para-fluorophenyl and the pyrrolidine nitrogen, and would have a reasonable expectation of success that the compounds will still antagonize 5-HT_2 to treat glaucoma and other ailments. See column 4, lines 38-43 and column 17, lines 51-63. Therefore, since only one group needs to be modified to take a disclosed species of Kuroita et al. to generate a compound of the instant claims, and that modification is sufficiently suggested within the reference, one of ordinary skill would have motivation to make the change to practice fully the invention of Kuroita et al. The rejection is maintained.

First, the Examiner's emphasis (see above) appears to suggest that In re Baird applies only where the claimed compounds are 'more complex' than those in the reference. That relates to the *facts* of Baird, but it does not represent the *rule* from Baird, which seems to lie in the conclusion of the sentence that states those facts: "we conclude that Knapp does not teach or fairly suggest the selection of bisphenol A." In re Baird, 29 USPQ2d 1550 (Fed. Cir. 1994). Thus the standard applied in Baird asked whether the reference 'teaches or fairly suggests' selection of what was claimed. See also the paragraph in Baird preceding that sentence: "While Knapp may suggest

certain complex bisphenol A derivatives, it does not *describe or suggest bisphenol A and therefore does not motivate the selection of bisphenol A*." Id. (emphasis added). Thus Baird provides a standard for examination that requires the Examiner to show that the prior art "describes or suggests" the invention as claimed, in order to establish a *prima facie* obviousness rejection, or that it "motivates the selection" of the invention as claimed. Simply stating that the reference discloses a particular species, which could be modified in a certain way, is not enough to establish obviousness under Baird, unless the reference is also shown to provide a reason to make the required changes. And simply showing that the modification remains within the disclosed genus does not show a motivation to make such modification.

Here, the Examiner selected which feature of the prior art species to modify from many possibilities, and the Examiner selected which modification to make from among many options. The reference discloses various features that could be modified and many ways to modify them, but has not been shown to provide any reason to select the changes required to arrive at the invention as claimed. (For example, the feature the Examiner chose to modify is D, and the specification says D is "optionally substituted linear or branched alkylene having 1 to 8 carbon atoms, and when D is branched alkylene, the carbon atom in the branched chain is optionally bonded further to Ar to form 4- to 8- membered ring, ..." Thus it provides many alternatives that could have been made, and the Examiner has not shown why a person of ordinary skill would have had reason to choose the particular one used in the analysis.) The Examiner's approach implies that nothing more is required to establish obviousness than showing that a modified structure that could be made remains within the scope of the claims, contradicting one *clear* rule from Baird: *a genus in the prior art does not render obvious all that it encompasses*. Obviousness is established by showing motivation to modify, not by merely showing that modification could be done while remaining within the scope of the genus.

The Examiner has shown that *once the applicant's invention is known*, it is possible to modify a species from the reference to fall within the scope of the broadest claim. That does not satisfy the burden placed on the Examiner by In re Baird to show that either the reference, or the general level of skill in the art, would have *suggested* to the person of ordinary skill to make the

particular selections and changes needed to get there. And Baird clearly demonstrates that claimed subject matter is not 'obvious' simply because it falls within a disclosed genus, if the teachings of that genus do not "motivate the selection" of what is now claimed. Thus the Examiner has not established a *prima facie* obviousness rejection under Baird.

In addition, claim 1 has been amended. The Examiner alleged in the rejection that only one feature (D) of a compound disclosed in the Kuroita reference would need to be changed in order to avoid the proviso in claim 1. The Examiner then concluded, "since only one group needs to be modified to take a disclosed species of Kuroita et al to generate a compound of the instant claims, and that modification is sufficiently suggested within the reference, one of ordinary skill would have motivation to make the change to practice fully the invention of Kuroita et al."

The proviso now present excludes the modified versions proposed by the Examiner: no modifications of D (which corresponds to L^2 in the present claims) could bring the compound of Kuroita within the scope of the claims, because the proviso no longer depends upon L^2. Thus the amendment overcomes the rationale for the rejection. As shown above, the Examiner has not shown motivation to make the proposed modification of the reference compound, and in view of the amendment, even making that modification would not provide a compound within the scope of the claims. Accordingly, this rejection can be withdrawn.

Claims 17 and 21-23 were alleged to be obvious based on In re Henze. The passage in Henze that the Examiner seems to rely on to support the rejection says this: "In effect, the nature of homologues and the close relationship the physical and chemical properties of one member of a series bears to *adjacent members* is such that a presumption of unpatentability arises against a claim directed to a composition of matter, the *adjacent homologue* of which is old in the art." 85 USPQ 261 (1950) (emphases added). The Examiner stated that Henze refers to 'adjacent members' of a series when citing it, but then *applied* it as though it justified rejecting any structure that can generally be characterized as a 'homolog'. But Henze does not say that all homologues are *prima facie* obvious regardless of how different they are in structure, only that an *adjacent* homolog of a species that is 'old in the art' may provide a *prima facie* basis for an obviousness rejection.

Nor does Henze show that homologs falling outside of a generally disclosed genus are a proper basis for an obviousness rejection: in Henze, "the adjacent homologue" was a specific compound that was disclosed and was thus "old in the prior art," it was not merely included within a broad *genus* in the prior art. In this case, the genus as disclosed and described in the prior art does not disclose or suggest *any* compounds that resemble the compounds of the claims, because such compounds are excluded by the proviso if they have $W = L^2\text{-}A^3$, and X = CH: the prior art genus does not even *encompass* such compounds. Rather, a prior art species having a 1-2 atom linker must be compared to a claim limitation requiring a 3-6 atom linker. The 1-2 atom linker of the example in Kuroita is clearly not "the adjacent homologue" of a 3-6 atom linker.

The Examiner relied upon a genus in the reference to effectively assert that all 'homologs' of a non-overlapping genus are obvious: that reasoning cannot be squared with Baird, which expressly shows that a disclosed genus does not even render obvious all compounds that it encompasses, surely it cannot render obvious all 'homologs' of all features of the genus! Describing a *genus*, without any sort of suggestion that anything outside the scope of the genus would be active, does not show that structures that are outside its scope are 'obvious'. As one of ordinary skill would recognize, **the genus was deliberately drafted to exclude compounds with linkers that fall within the scope of the present claims. The person of ordinary skill would understand that the drafter of the Kuroita genus did not assert that other linkers would have the claimed activity**. Thus Henze does not support the conclusion that the claim limitation 3-6 is *prima facie* obvious over a species with a 1-atom linker, or that a genus limitation is a proper basis for a rejection of homologs.

The Advisory Action

In the Advisory Action, the Examiner indicated that the modified proviso did not overcome the obviousness rejection because "Kuroita et al discloses compounds with the clearly adjacent member where D is a two atom linker instead of the three atom linker claimed. Additionally, Kuroita et al. teaches a synthesis example that shows facile synthesis of the entire claimed genus, thereby making the synthesis of the instantly claimed compounds obvious."

The Applicants disagree with the first assertion: with the amendment to the proviso, the proviso has been broadened in scope so that it excludes compounds wherein L^1 contains fewer than three linking atoms if X^1 is CH and W is L^2-A^3. 'D' in the Kuroita compounds corresponds to L^2 in the present claims. The example that the Examiner relied upon for the previous rejection is a structure with just a single linking atom (a carbonyl carbon) to correspond to L^1 in the present claims. The proviso excludes all of the Kuroita compounds having a linker L^1 shorter than three atoms. Thus the compound in Kuroita is not an adjacent member to the claimed genus, it is two atoms removed in length from the claim scope. Moreover, the corresponding feature in Kuroita is referred to in Kuroita as "X", and the entire *genus* described in Kuroita allows X to have only one or at most two linking atoms, which are specifically defined: X must be selected from C=O, C=S, NH-C=O, SO, and SO_2. Col. 4 of Kuroita. Thus a compound within the scope of the present claims that has W = L^2-A^3, and X^1 = CH must have a linker L^1 that is outside the scope of the linkers that Kuroita indicate are useful for its purposes. [Note: the only R^1 group in Kuorita's genus that appears potentially relevant is its formula (2), in which the feature corresponding to X^1 of the instant claims is CH and there is no provision for it to be substituted. The group –D-Ar in Kuroita corresponds to W in the instant claims, so Kuroita's genus can only resemble the compounds of formula (1) when W in formula (1) is L^2-A^3. Thus "W = L^2-A^3, and X^1 = CH" is believed to cover all of the relevant genus from Kuroita; so requiring the linker L^1 to be three or more atoms in length in such compounds excludes ***all*** of the genus and species of Kuroita.] Moreover, the few disclosed species in Kuroita that appear closest to the limitations in the proviso have only a one-atom linker corresponding to L^1, so no species in Kuroita is adjacent to the 'at least three-atom' L^1 linker.

In addition, the brief explanation in the Advisory Action mentions the reaction schemes in Kuroita as allegedly providing a "facile synthesis of the entire claimed genus." However, the only synthesis scheme in Kuroita that appears potentially relevant to compounds where L^1 is longer than one atom is Synthesis Method 6, which shows a two-atom linker (NH-C=O) corresponding to L^1. Col. 14. That linker would still have to be elongated by one atom to fall within the scope of the current claims. In that example, D and R^1 are generic features that may or may not fall within the scope of the present claims, depending on how they are selected. Since most of the R^1 groups in

Kuroita are *not* within the scope of the present claims (see cols. 2-3), it would require a judicious selection of both D and R^1 *in addition* to modification of the linker to arrive at the claimed invention. Moreover, the associated text describing formation of that two-atom linker in that synthesis scheme indicates that it is suitable only for making compounds wherein X is NH-C=O; Kuroita does not suggest that it would be suitable for making other relevant linkers. So the synthesis methods, while generally suited for making the compounds within the scope of Kuroita's genus, do not illustrate making compounds within the scope of the present claims, and they are not described as suitable for making compounds having a L^1 linker that is longer than two atoms. Thus both 'picking and choosing' of particular groups R^1 and D, which are broadly described, *and* extension of the linking group shown in Synthesis Method 6 would be required to arrive at a compound within the present claims. Accordingly, based on Kuroita, the person of ordinary skill would not have had a reason to make a compound within the scope of the present claims, would not have been enabled by Kuroita's synthesis schemes to make such a compound, and would not have reasonably *expected* it to have the biological activity sought by the compounds in Kuorita. Thus Kuroita does not support a *prima facie* case for an obviousness rejection of the claims as presented, and this rejection should be withdrawn.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 381092001600. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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